IN THE CLAIMS

We Claim:

1. (Currently Amended) A method comprising:

a) reacting two or more samples, each sample comprising one or more reactive analytes, with a different labeling reagent of a set of labeling reagents to thereby produce two or more differentially and ~~isoborically~~ isobarically labeled samples each comprising one or more labeled analytes wherein the different labeling reagents of the set each comprise the formula:

RP-X-LK-Y-RG

or a salt thereof wherein;

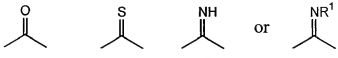
i) RG is a reactive group that is an electrophile and that is capable of reacting with one or more of the reactive analytes of the sample;

ii) RP is a reporter moiety that comprises a fixed charge or that is ionizable, wherein the gross mass of each reporter is different for each reagent of the set;

iii) LK is a linker moiety that links the reactive group and the reporter group, wherein:

a) the mass of the linker compensates for the difference in gross mass between the reporters for the different labeling reagents of the set such that the aggregate gross mass of the reporter and linker combination is the same for each reagent of the set; and

b) the linker comprises at least one heavy atom isotope and has the formula:



wherein R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups

independently comprise linked hydrogen, deuterium and/or fluorine atoms;

iv) X is a bond between an atom of the reporter and an atom of the linker;

v) Y is a bond between an atom of the linker and an atom of the reactive group, wherein, once the labeling reagent is reacted with the reactive analyte, bond Y links the linker to the analyte; and

b) mixing two or more of the differentially labeled samples, or a portion thereof, and optionally one or more calibration standards to thereby produce a sample mixture.

2. (Original) The method of claim 1, further comprising:

c) performing a first mass spectrometric analysis on the sample mixture, or a fraction thereof;

d) treating selected ions of labeled analytes from the first mass spectrometric analysis to dissociative energy levels to thereby form ionized reporter moieties and ionized daughter fragment ions of at least some of the selected ions; and

e) performing a second mass analysis of the selected ions, the ionized reporter moieties and the daughter fragment ions, or a fraction thereof.

3. (Original) The method of claim 2, further comprising:

f) determining the gross mass and relative amount of each reporter moiety in the second mass analysis and the gross mass of the daughter fragment ions.

4. (Original) The method of claim 3, further comprising repeating steps (d) through (f) one or more times on selected ions of labeled analytes at a different selected mass to charge ratio.

5. (Original) The method of claim 4, further comprising repeating steps (a) through (f) one or more times, each time with a different fraction of the sample mixture.

6. (Original) The method of claim 1, wherein the two or more samples are the products of an enzymatic digestion reaction.

7. (Original) The method of claim 6, wherein the two or more samples are products of a proteolytic digestion reaction.

8. (Original) The method of claim 7, wherein the proteolytic enzyme is trypsin, papain, pepsin, ArgC, LysC, V8 protease, AspN, pronase, chymotrypsin or carboxypeptidease C.

9. (Withdrawn) The method of claim 1, wherein each sample is a crude or processed cell lysate, a body fluid, a tissue extract or a cell extract.

10. (Withdrawn) The method of claim 1, wherein each sample is a fraction from a separations process.

11. (Withdrawn) The method of claim 10, wherein the separations process is a chromatographic separation or an electrophoretic separation.

12. (Withdrawn) The method of claim 9, wherein the body fluid is blood, urine, spinal fluid, cerebral fluid, amniotic fluid, lymph fluid or a fluid from a glandular secretion.

13. (Withdrawn) The method of claim 1, wherein the one or more analytes are proteins, nucleic acid molecules, carbohydrates, lipids, steroids or small molecules of less than 1500 daltons.

14. (Original) The method of claim 1, wherein the one or more of the analytes are peptides.

15. (Original) The method of claim 14, wherein the peptides are formed by digestion of at least one protein.

16. (Withdrawn) The method of claim 15, wherein the peptides are formed by digestion of the total protein component of a crude whole cell lysate.

17. (Original) The method of claim 1, wherein the reactive group of each reagent of the set is prepared *in-situ* for reaction with the reactive analytes.

18. (Withdrawn) The method of claim 17, wherein the reactive group of the each reagent of the set is a carboxylic acid group that has been activated with a water-soluble carbodiimide.

19. (Withdrawn) The method of claim 18, wherein the water-soluble carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC).

20. (Original) The method of claim 1, wherein the reactive group of each reagent of the set is an amine reactive active ester group.

21. (Original) The method of claim 20, wherein the active ester is a N-hydroxysuccinimidyl ester, a N-hydroxysulfosuccinimidyl ester, a pentafluorophenyl ester, a 2-nitrophenyl ester, a 4-nitrophenyl ester, a 2,4-dinitrophenylester or a 2,4-dihalophenyl ester.

22. (Original) The method of claim 1, wherein the reporter has a gross mass of less than 250 daltons.

23. (Original) The method of claim 1, wherein the reporter is not a polymer.

24. (Original) The method of claim 1, wherein the reporter is not a biological polymer.

25. (Original) The method of claim 1, wherein the reporter is a substituted or unsubstituted morpholine, piperidine or piperazine compound, or a salt thereof.

26. (Withdrawn) The method of claim 1, wherein the reporter is a carboxylic acid, sulfonic acid or phosphoric acid group-containing compound, or a salt thereof.

27. (Original) The method of claim 1, wherein the reporter moiety does not substantially sub-fragment under conditions used to determine the analyte.

28. (Original) The method of claim 1, wherein the linker is a carbonyl or thiocarbonyl group.

29. (Original) The method of claim 1, wherein bonds X and Y fragment in at least a portion of the labeled analytes when subjected to dissociative energy levels.

30. (Withdrawn) The method of claim 1, wherein the reporter does not substantially sub-fragment under conditions of dissociative energy applied to cause fragmentation of at least a portion of both bonds X and Y of a labeled analyte in a mass spectrometer

31. (Withdrawn) The method of claim 1, wherein the linker undergoes neutral loss under conditions of applied dissociative energy that causes the fragmentation of both bonds X and Y in a mass spectrometer.

32. (Withdrawn) The method of claim 1, wherein, under conditions of dissociative energy applied in a mass spectrometer, the fragmentation of one of bonds X or Y results in the fragmentation of the other of bonds X or Y.

33. (Withdrawn) The method of claim 1, wherein under conditions of dissociative energy applied in a mass spectrometer, bond X is less prone to fragmentation as compared with bond Y.

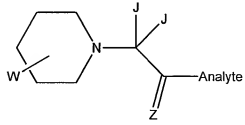
34. (Original) The method of claim 1, wherein under conditions of dissociative energy applied in a mass spectrometer, bond X is less prone to fragmentation as compared with the peptide bond of a Z-pro amino acid dimer or Z-asp amino acid dimer, wherein Z is any natural amino acid, pro is proline and asp is aspartic acid.

35. (Withdrawn) The method of claim 1, wherein the one or more differentially labeled analytes each comprise an isomeric label that identifies the sample from which it originated.

36. (Original) The method of claim 1, wherein the one or more differentially labeled analytes each comprise an isobaric label that identifies the sample from which it originated.

37. (Original) The method of claim 36, wherein the label of each isobarically labeled analyte is a 5, 6 or 7 membered heterocyclic ring comprising a ring nitrogen atom that is N-alkylated with a substituted or unsubstituted acetic acid moiety to which the analyte is linked through the carbonyl carbon of the N-alkyl acetic acid moiety, wherein each different label comprises one or more heavy atom isotopes.

38. (Withdrawn) The method of claim 37, wherein the isobarically labeled analytes in the sample mixture each comprise the formula:



wherein;

a) Z is O, S, NH or NR^1;

b) each J is the same or different and is H, deuterium (D), R^1, OR^1, SR^1, NHR^1, $N(R^1)_2$, fluorine, chlorine, bromine or iodine;

c) W is an atom or group that is located ortho, meta or para to the ring nitrogen and is NH, N-R^1, N-R^2, P-R^1, P-R^2, O or S;

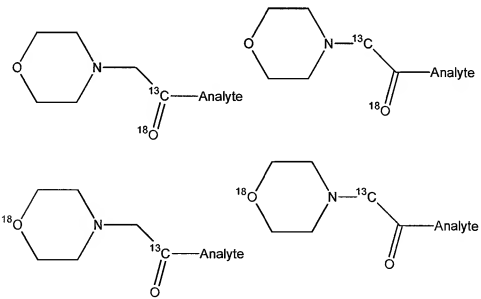
d) each carbon of the heterocyclic ring has the formula CJ_2;

e) each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms; and

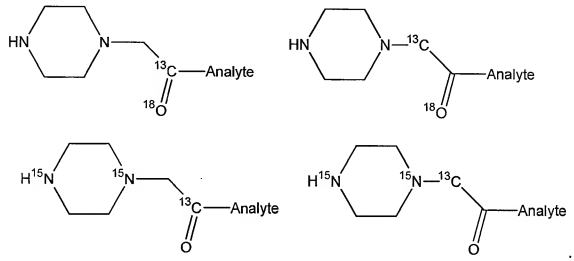
f) R^2 is an amino alkyl, hydroxy alkyl, thio alkyl group or a cleavable linker that cleavably links the reagent to a solid support wherein the amino alkyl, hydroxy alkyl or thio alkyl group comprises one to eight carbon atoms, which may optionally contain a heteroatom or a substituted or unsubstituted aryl group, and wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

39. (Withdrawn) The method of claim 36, wherein the isobarically labeled analytes are peptides.

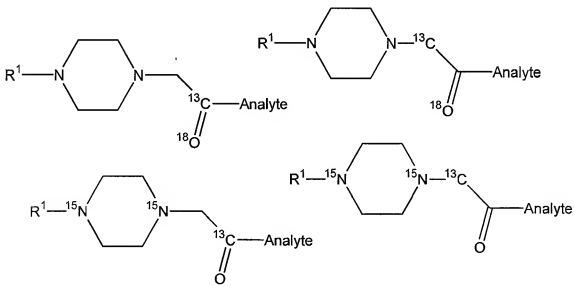
40. (Withdrawn) The method of claim 38, wherein the sample mixture comprises one or more isobarically labeled analytes of the formula:



41. (Withdrawn) The method of claim 38, wherein the sample mixture comprises one or more isobarically labeled analytes of the formula:

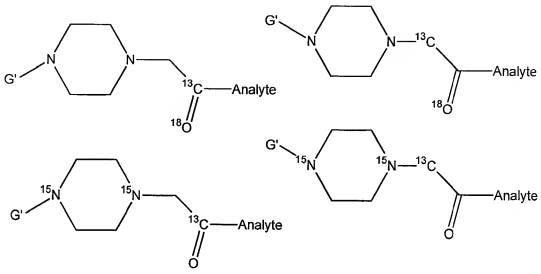


42. (Original) The method of claim 38, wherein the sample mixture comprises one or more isobarically labeled analytes of the formula:



wherein each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

43. (Original) The method of claim 38, wherein the sample mixture comprises one or more isobarically labeled analytes of the formula:



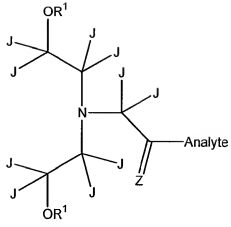
wherein:

a) G' is an amino alkyl, hydroxy alkyl or thio alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms;

b) each carbon of the heterocyclic ring has the formula CJ_2, wherein each J is the same or different and is selected from the group consisting of: H, deuterium (D), R^1, OR^1, SR^1, NHR^1, $N(R^1)_2$, fluorine, chlorine, bromine and iodine; and

c) each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

44. (Withdrawn) The method of claim 36, wherein the isobarically labeled analytes in the sample mixture each comprise the formula:



wherein:

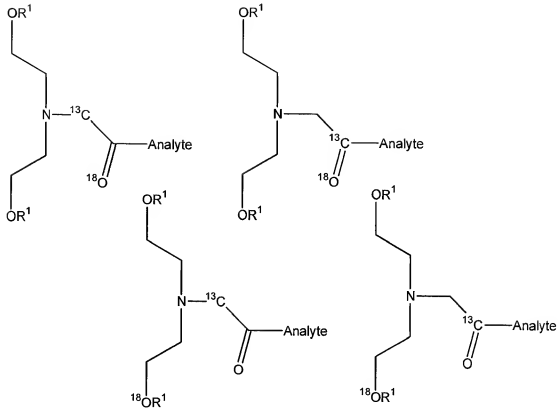
a) Z is O, S, NH or NR^1;

b) each J is the same or different and is selected from the group consisting of: H, deuterium (D), R^1, OR^1, SR^1, NHR^1, $N(R^1)_2$, fluorine, chlorine, bromine and iodine;

c)each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

45. (Withdrawn) The method of claim 44, wherein the isobarically labeled analytes are peptides.

46. (Withdrawn) The method of claim 44, wherein the sample mixture comprises one or more isobarically labeled analytes of the formula:



wherein each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

47. (Original) The method of claim 1, wherein each different labeling reagent of the set is support bound and is linked to the support through a cleavable linker such that each different sample is reacted with a support carrying a different labeling reagent; and the method further comprises, before performing step (b);

i) optionally washing the resin to remove components of the sample that do not react with the reactive group of the labeling reagent; and

ii) cleaving the cleavable linker to thereby collect the two or more differentially labeled samples, each sample comprising one or more labeled analytes wherein the labeled analytes associated with a particular

sample are identifiable and/or quantifiable by the unique reporter linked thereto.

48. (Original) The method of claim 47, wherein each different labeling reagent of the set is a solid support of the formula:

E-F-RP-X-LK-Y-RG

wherein;

i) RG is a reactive group that is a nucleophile or an electrophile and that is capable of reacting with one or more of the reactive analytes of the samples;

ii) RP is a reporter moiety that comprises a fixed charge or that is ionizable, wherein the gross mass of each reporter is different for each reagent of the set;

iii) LK is a linker moiety that links the reactive group and the reporter group, wherein the mass of the linker compensates for the difference in gross mass between the reporters for the different labeling reagents of the set such that the aggregate gross mass of the reporter and linker combination is the same for each reagent of the set;

iv) X is a bond between an atom of the reporter and an atom of the linker;

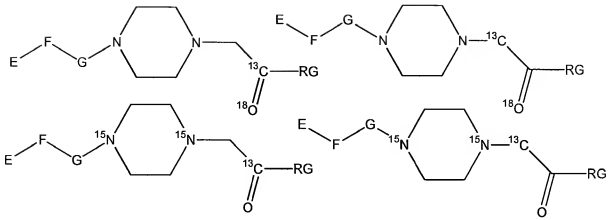
v) Y is a bond between an atom of the linker and an atom of the reactive group, wherein, once the labeling reagent is reacted with the reactive analyte, bond Y links the linker to the analyte;

vi) bonds X and Y fragment in at least a portion of the labeled analytes when subjected to dissociative energy levels;

vii) E is a solid support; and

viii) F is a cleavable linker linked to the solid support and cleavably linked to the reporter.

49. (Original) The method of claim 48, wherein the set of labeling reagents comprises one or more of the following support bound labeling reagents:



wherein:

i) RG is a reactive group that is a nucleophile or an electrophile and that is capable of reacting with one or more of the reactive analytes of the samples;

ii) E is a solid support;

iii) F is a cleavable linker linked to the solid support and cleavably linked to the reporter;

iv) G is an amino alkyl, hydroxy alkyl or thio alkyl group, cleavably linked to the cleavable linker wherein the amino alkyl, hydroxy alkyl or thio alkyl group comprises one to eight carbon atoms, which may optionally contain a heteroatom or a substituted or unsubstituted aryl group, and wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms;

v) each carbon of the heterocyclic ring has the formula CJ_2, wherein each J is the same or different and is selected from the group consisting of H, deuterium (D), R^1, OR^1, SR^1, NHR^1, $N(R^1)_2$, fluorine, chlorine, bromine and iodine; and

vi) each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the

alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

50. (Original) The method of claim 47, wherein the support is composed of polystyrene, polyethylene, polypropylene, polyfluoroethylene, polyethyleneoxy, polyacrylamide, glass, silica, controlled-pore-glass (CPG), or reverse-phase silica.

51. (Original) The method of claim 47, wherein the solid support is in the form of beads, spheres, particles, granules, a gel, a membrane or a surface.

52. (Original) The method claim 1, further comprising:
c) digesting each sample with at least one enzyme to partially, or fully, degrade components of the sample prior to performing step (a).

53. (Original) The method of claim 52, wherein the enzyme is a proteolytic enzyme.

54. (Original) The method of claim 53, wherein the proteolytic enzyme is trypsin, papain, pepsin, ArgC, LysC, V8 protease, AspN, pronase, chymotrypsin or carboxypeptidease C.

55. (Original) The method of claim 1, wherein the method further comprises:
c)separating the sample mixture.

56. (Original) The method of claim 55, wherein the separation is performed by chromatography.

57. (Original) The method of claim 56, wherein the chromatographic separation method is normal phase chromatography, reversed-phase chromatography, ion-exchange chromatography, size exclusion chromatography or affinity chromatography.

58. (Original) The method of claim 55, wherein the separation is performed electrophoretically.

59. (Original) The method of claim 28, wherein the electrophoretic separation is a 1D electrophoretic separation, a 2D electrophoretic separation or a capillary electrophoretic separation.

60. (Original) The method of claim 1, wherein the method further comprises:
c) digesting each sample with at least one enzyme to partially, or fully, degrade components of the sample prior to performing step (a); and
d) separating the sample mixture.

61. (Original) The method of claim 60, wherein the enzyme is a proteolytic enzyme.

62. (Original) The method of claim 61, wherein the proteolytic enzyme is trypsin, papain, pepsin, chymotrypsin or carboxypeptidease C.

63. (Original) The method of claim 60, wherein the separation is performed by chromatography.

64. (Original) The method of claim 63, wherein the chromatographic separation method is normal phase chromatography, reversed-phase chromatography, ion-exchange chromatography, size exclusion chromatography or affinity chromatography.

65. (Original) The method of claim 60, wherein the separation is an electrophoretic separation.

66. (Original) The method of claim 65, wherein the electrophoretic separation is a 1D electrophoretic separation, a 2D electrophoretic separation or a capillary electrophoretic separation.

67. (Original) The method of claim 3, wherein the identity of the labeled analyte associated with the selected mass to charge ratio is determined by analysis of the daughter fragment ions.

68. (Original) The method of claim 67, wherein the relative amount of each reporter in the second mass analysis is determined with respect to the other reporters.

69. (Original) The method of claim 68, wherein the relative amount of each reporter associated with the identified analyte is correlated with the amount of each sample added to form the sample mixture to thereby determine the relative amount of the analyte in each of two or more of the samples combined to form the mixture.

70. (Original) The method of claim 69, wherein:

(i) the sample mixture comprises a known amount of a calibration standard for the identified analyte and the absolute amount of each reporter is determined with reference to the amount of reporter associated with the calibration standard; and

(ii) the absolute amount of the identified analyte in each different sample of the sample mixture is determined with reference to the amount of each reporter.

71. (Original) The method of claim 69, further comprising repeating steps (d) through (f), on selected ions of labeled analytes at a different selected mass to charge ratio, one or more times to thereby identify and/or determine the relative amount of one or more other analytes in each of two or more of the samples combined to form the sample mixture.

72. (Original) The method of claim 70, further comprising repeating steps (d) through (f), on selected ions of labeled analytes at a different selected mass to charge ratio, one or more times to thereby identify and/or determine the absolute amount of one

or more other analytes in each of two or more of the samples combined to form the sample mixture.

73. (Original) The method of claim 69, wherein the analytes are peptides and the identity and relative amount of one or more proteins in each of two or more of the samples combined to form the sample mixture is determined based upon the identity and relative amount of the one or more peptides in each of two or more of the samples combined to form the sample mixture.

74. (Original) The method of claim 70, wherein the analytes are peptides and the identity and relative amount of one or more proteins in each of two or more of the samples combined to form the sample mixture is determined based upon the identity and absolute amount of the one or more peptides in each of two or more of the samples combined to form the sample mixture.

75. (Original) The method of claim 3, further comprising:

g) digesting each sample with at least one enzyme to partially, or fully, degrade components of the sample prior to performing step (a); and

h) separating the sample mixture prior to performing step (c).

76. (Original) The method of claim 75, wherein the enzyme is a proteolytic enzyme.

77. (Original) The method of claim 76, wherein the proteolytic enzyme is trypsin, papain, pepsin, chymotrypsin or carboxypeptidease C.

78. (Original) The method of claim 75, wherein the separation is performed by chromatography.

79. (Original) The method of claim 78, wherein the chromatographic separation method is normal phase chromatography, reversed-phase chromatography, ion-exchange chromatography, size exclusion chromatography or affinity chromatography.

80. (Original) The method of claim 75, wherein the separation is an electrophoretic separation.

81. (Original) The method of claim 80, wherein the electrophoretic separation is a 1D electrophoretic separation, a 2D electrophoretic separation or a capillary electrophoretic separation.

82. T(Original) he method of claim 75, wherein the identity of the labeled analyte associated with the selected mass to charge ratio is determined by analysis of the daughter fragment ions.

83. (Original) The method of claim 82, wherein the relative amount of each reporter in the second mass analysis is determined with respect to the other reporters.

84. (Original) The method of claim 83, wherein the relative amount of each reporter associated with the identified analyte is correlated with the amount of each sample added to form the sample mixture to thereby determine the relative amount of the analyte in each of two or more of the samples combined to form the mixture.

85. (Original) The method of claim 84, wherein:

(i) the sample mixture comprises a known amount of a calibration standard for the identified analyte and the absolute amount of each reporter is determined with reference to the amount of reporter associated with the calibration standard; and

(ii) the absolute amount of the identified analyte in each different sample of the sample mixture is determined with reference to the amount of each reporter.

86. (Original) The method of claim 84, further comprising repeating steps (d) through (f), on selected ions of labeled analytes at a different selected mass to charge ratio, one or more times to thereby identify and/or determine the relative amount of one or more other analytes in each of two or more of the samples combined to form the sample mixture.

87. (Original) The method of claim 85, further comprising repeating steps (d) through (f), on selected ions of labeled analytes at a different selected mass to charge ratio, one or more times to thereby identify and/or determine the absolute amount of one or more other analytes in each of two or more of the samples combined to form the sample mixture.

88. (Original) The method of claim 84, wherein the analytes are peptides and the identity and relative amount of one or more proteins in each of two or more of the samples combined to form the sample mixture is determined based upon the identity and relative amount of the one or more peptides in each of two or more of the samples combined to form the sample mixture.

89. (Original) The method of claim 85, wherein the analytes are peptides and the identity and relative amount of one or more proteins in each of two or more of the samples combined to form the sample mixture is determined based upon the identity and absolute amount of the one or more peptides in each of two or more of the samples combined to form the sample mixture.

90. (Currently Amended) A mixture comprising at least two ~~isobarically~~ isobarically labeled analytes, wherein each of the two labeled analytes originates from a different sample combined to form the mixture and each comprises the formula:

RP-X-LK-Y-Analyte

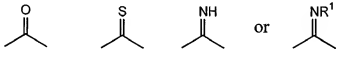
or a salt thereof wherein;

a) RP is a reporter moiety that comprises a fixed charge or that is ionizable, wherein the gross mass of each reporter is different for each sample;

b) LK is a linker moiety that links the reactive group and the reporter group, wherein:

i) the mass of the linker compensates for the difference in gross mass between the reporters for the different labeling reagents of the set such that the aggregate gross mass of the reporter and linker combination is the same for each reagent of the set; and

ii) the linker comprises at least one heavy atom isotope and has the formula:



wherein R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms;

c) X is a bond between an atom of the reporter and an atom of the linker;

d) Y is a bond between an atom of the linker and an atom of the analyte.

91. (Original) The mixture of claim 90, wherein both bonds X and Y fragment in at least a portion of the labeled analytes when subjected to dissociative energy levels.

92. (Original) The mixture of claim 90, wherein under conditions of dissociative energy applied in a mass spectrometer, the fragmentation of one of bonds X or Y results in the fragmentation of the other of bonds X or Y.

93. (Withdrawn) The mixture of claim 90, wherein under conditions of dissociative energy applied in a mass spectrometer, bond X is less prone to fragmentation as compared with bond Y.

94. (Original) The mixture of claim 90, wherein under conditions of dissociative energy applied in a mass spectrometer, bond X is less prone to fragmentation as compared with the peptide bond of a Z-pro amino acid dimer or Z-asp amino acid dimer, wherein Z is any natural amino acid, pro is proline and asp is aspartic acid

95. (Original) The mixture of claim 90, wherein one or more of the analytes are peptides.

96. (Withdrawn) The mixture of claim 90, wherein one or more of the analytes are proteins.

97. (Withdrawn) The mixture of claim 90, wherein one or more of the analytes are nucleic acid molecules.

98. (Original) The mixture of claim 90, wherein the reporter is a substituted or unsubstituted morpholine, piperidine or piperazine compound, or a salt thereof.

99. (Withdrawn) The mixture of claim 90, wherein the reporter is a carboxylic acid, sulfonic acid or phosphoric acid group containing compound, or a salt thereof.

100. (Original) The mixture of claim 90, wherein the reporter has a gross mass of less than 250 daltons.

101. (Withdrawn) The mixture of claim 90, wherein the reporter does not substantially sub-fragment under conditions of dissociative energy applied to cause fragmentation of at least a portion of both bonds X and Y of a labeled analyte in a mass spectrometer.

102. (Original) The mixture of claim 90, wherein the reporter is not a polymer.

103. (Original) The mixture of claim 90, wherein the reporter is not a biological polymer.

104. (Original) The mixture of claim 90, wherein the linker is a carbonyl or thiocarbonyl group.

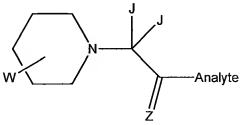
105. (Withdrawn) The mixture of claim 90, wherein the linker LK undergoes neutral loss under conditions of applied dissociative energy that causes the fragmentation of both bonds X and Y in a mass spectrometer.

106. (Withdrawn) The mixture of claim 90, wherein the at least two labeled analytes each comprise an isomeric label.

107. (Original) The mixture of claim 90, wherein the at least two labeled analytes each comprise an isobaric label.

108. (Original) The mixture of claim 107, wherein the at least two labeled analytes each comprise an isobaric label that is a 5, 6 or 7 membered heterocyclic ring comprising a ring nitrogen atom that is N-alkylated with a substituted or unsubstituted acetic acid moiety to which the analyte is linked through the carbonyl carbon of the N-alkyl acetic acid moiety, wherein each different label comprises one or more heavy atom isotopes.

109. (Original) The mixture of claim 108, wherein each of the at least two isobarically labeled analytes in the mixture comprise the formula:



wherein;

a) Z is O, S, NH or NR^1;

b) each J is the same or different and is H, deuterium (D), R^1, OR^1, SR^1, NHR^1, $N(R^1)_2$, fluorine, chlorine, bromine or iodine;

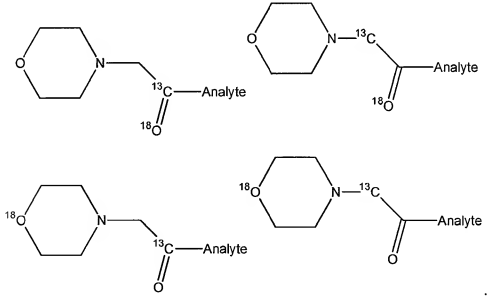
c) W is an atom or group that is located ortho, meta or para to the ring nitrogen and is NH, N-R^1, N-R^2, P-R^1, P-R^2, O or S;

d) each carbon of the heterocyclic ring has the formula CJ_2;

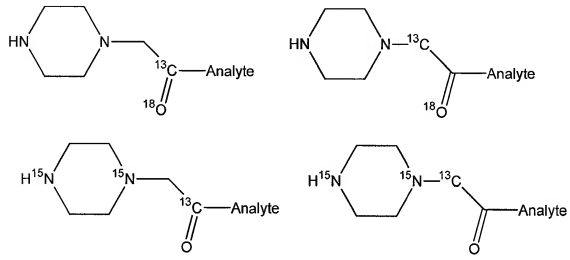
e) each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms; and

f) R^2 is an amino alkyl, hydroxy alkyl, thio alkyl group or a cleavable linker that cleavably links the reagent to a solid support wherein the amino alkyl, hydroxy alkyl or thio alkyl group comprises one to eight carbon atoms, which may optionally contain a heteroatom or a substituted or unsubstituted aryl group, and wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

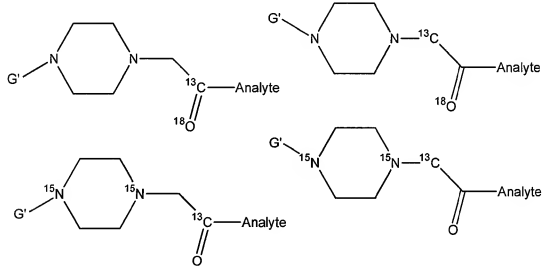
110. (Withdrawn) The mixture of claim 109, wherein the mixture comprises one or more isobarically labeled analytes of the formula:



111. (Withdrawn) The mixture of claim 109, wherein the mixture comprises one or more isobarically labeled analytes of the formula:



112. (Original) The mixture of claim 109, wherein the mixture comprises one or more isobarically labeled analytes of the formula:



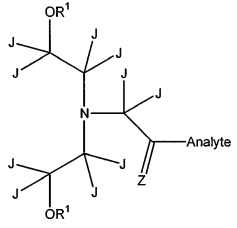
wherein:

a) G' is an amino alkyl, hydroxy alkyl or thio alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms;

b) each carbon of the heterocyclic ring has the formula CJ_2, wherein each J is the same or different and is selected from the group consisting of: H, deuterium (D), R^1, OR^1, SR^1, NHR^1, $N(R^1)_2$, fluorine, chlorine, bromine and iodine; and

c)each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

113. (Withdrawn) The mixture of claim 107, wherein the mixture comprises one or more isobarically labeled analytes of the formula:



wherein:

a) Z is O, S, NH or NR^1;

b) each J is the same or different and is selected from the group consisting of: H, deuterium (D), R^1, OR^1, SR^1, NHR^1, $N(R^1)_2$, fluorine, chlorine, bromine and iodine;

c)each R^1 is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms.

114. (Original) The mixture of 90, further comprising one or more calibration standards.